REMARKS

Status of the claims

Claim 13 has been canceled in the amendment filed 5/28/09. Claims 3-5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected claims.

Withdrawn objections and rejections

Applicant acknowledges that the following previous rejections and objections are withdrawn in light of applicants amendments filed on 5/28/09:

(i) the objection to the title of the invention;

(ii) the rejection of claims 13 under 35 U.S.C. 101; and

(iii) the rejection of claim 8, under 35 U.S.C. 112, first paragraph;

(iv) the rejection of claims 1-2, and 6-13, under 35 U.S.C. 112, second paragraph;

(v) the rejection of claims 1-2, 6-7, and 9-13, under 35 U.S.C. § 103 as being unpatentable over Kishimoto et al (US Patent No. 5,888,510) in view of Raynauld et al. (2003);

(vi) the rejection of claim 7 under 35 U.S.C. 103(a) as being unpatentable over Kishimoto et al. (US Patent No. 5,888,510) in view of Raynauld et al. (2003) as applied to claims 1-2, 6, and 9-13, above, and further in view in of Queen et al. (U.S. Patent No. 5,530,101).

Claim Rejections - 35 USC § 103

The Examiner has raised a new rejection of Claims 1-2, 6, and 9-10, under 35 U.S.C. § 103 as allegedly being unpatentable over Kishimoto et al (US Patent No. 5,888,510) in view of Kaneko et al. (2000).

The Examiner asserts Kishimoto et al. teach a method for inhibiting synovial cell growth by administering to a patient polyclonal or monoclonal antibodies to IL-6 and also teach a method of treating **chronic rheumatoid arthritis** by administering to a patient IL-6 antagonists including polyclonal or monoclonal antibodies to the IL-6 receptor. The Examiner concludes Kishimoto discloses that if a cytokine causes a disease, an antibody to the cytokine will block the signal transduction by the cytokine, inhibit the cytokines

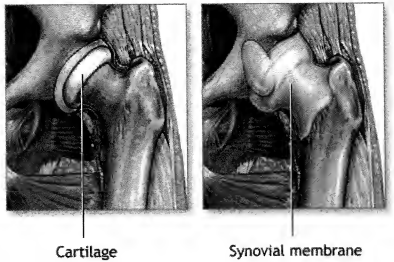
biological activity and has an alleviating and therapeutic effect on the symptoms of the disease.

The Examiner asserts Kaneko et al teach that higher concentrations of inflammatory cytokine IL-6 levels were found in serum and synovial fluid of patients with osteoarthritis. The Examiner freely concedes Kaneko et al. do not disclose a method of administering IL-6 antibodies to treat osteoarthritis in a patient.

The Examiner asserts, it would have been *prima facie* obvious to one having ordinary skill in the art, from the method of Kishimoto to administer IL-6 antibodies to a patient for the treatment of osteoarthritis to obtain the known functions and advantages thereof as per the teachings of Kishimoto et al because Kaneko et al teach that elevated levels of the inflammatory cytokine IL-6 are found in osteoarthritic patients and would have been motivated to administer the IL-6 antibodies in the treatment of osteoarthritis. The Examiner asserts administration of IL-6 antibodies would be effective therapy for osteoarthritis because Kishimoto teaches that administration of IL-6 antibodies reduces inflammation caused by IL-6 in patient populations with rheumatoid arthritis since both RA and OA are chronic inflammatory diseases.

Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obvious. The Examiner freely admits Kishimoto et al. & Kaneko et al. do not disclose a method of treating osteoarthritis by administering an IL- 6 antibody. The Examiner concludes since IL-6 levels are elevated in synovial fluids of patients with RA and that an IL-6 receptor antibody inhibits synovial cell growth that because IL-6 levels are also elevated in synovial fluids of patients with OA that an IL-6 antibody will predictably treat OA. However, this argumentation is flawed for several reasons. First, not only are IL-6 levels elevated in synovial fluids in RA and OA but also are many other inflammatory mediators including cytokines including but not limited to IL-1ß, IL-6, IL-8, IL-18, TNF-a, TNF-a converting enzyme (TACE), PGE2, COX-2, nuclear factor kappa B (NF-?B), NO, monocyte chemoattractant protein-1 (MCP-1), TGF-ß, myeloperoxidase, heat shock protein 70 (HSP70), as well as the matrix metalloproteinases (MMP)-1, -3, -9, -10, and -13. Second, IL-6 and IL-8 levels are significantly higher in RA than in OA (Kaneko, p 71 Abstract). Third, the Examiner's characterization of RA and OA as chronic inflammatory diseases is not correct since OA is noninflammatory degenerative type of arthritis marked by degradation of articular cartilage and the subchondral bone next to it and the overgrowth of bone at the margins, while RA is a chronic systemic inflammatory

disorder characterized by inflammatory changes throughout the body's connective tissues and may affect many tissues and organs, including inflammation of synovial membranes that line joints.



Given the distinct differences between RA and OA, the large number of inflammatory mediators that are elevated, and the significant differences in the levels of IL-6 in RA versus OA one skilled in the art would not have been motivated to treat OA with and IL-6 antibody and the results were not reasonably predicted. At best Kaneko et al. relied upon by the Examiner relies concludes "*determination of IL-6 and IL-8 levels is useful for understanding of disease status and making a clinical diagnosis of OA and RA*" (page 79, last paragraph) not a preferred target for OA treatment. No evidence is provided in either Kishimoto et al or Kaneko et al. that elevated IL-6 causes OA as asserted by the Examiner. Therefore, it is submitted that the Office has failed to establish a *prima facie* case of obviousness.

The Examiner has made a new rejection of Claim 7 under 35 U.S.C. 103(a) as being unpatentable over Kishimoto et al (US Patent No. 5,888,510) in view of Kaneko et al. (2000) as applied to claims 1-2, 6, 9-10, above, and further in view of Queen et al. (U.S. Patent No. 5,530,101).

The Examiner relies on Queen to teach humanization of antibodies. The insufficiencies of Kishimoto et al and Kaneko et al have been set forth above. Queen et al. does not overcome the insufficiencies of Kishimoto et al. or Kaneko et al. with respect administering an IL-6 antibody to treat osteoarthritis. It is submitted that the Office has failed to establish a *prima facie* case of obviousness.

The Examiner has made a new rejection of Claims 11-12, under 35 U.S.C. § 103 as being unpatentable over Kishimoto et al (US Patent No. 5,888,510) in view of Kaneko et al. (2000) and Karim et al. (US Patent No. 5,888,510).

The Examiner relies on Karim et al to teach administration of agents, such as celecoxib or ibuprofen for pain in osteoarthritic patients. The insufficiencies of Kishimoto et al and Kaneko et al have been set forth above. Karim et al. does not overcome the insufficiencies of Kishimoto et al. or Kaneko et al. with respect to administering an IL-6 antibody to treat osteoarthritis. It is submitted that the Office has failed to establish a *prima facie* case of obviousness.

CONCLUSIONS

Applicant submits that the FINAL REJECTION is premature because the Examiner has failed to show why the rejections weren't made previously. Withdrawal of the FINAL REJECTION and consideration of the response herewith is requested. Applicants submit that the present invention is now in condition for allowance. No new matter has been added. Early allowance of all pending claims is respectfully solicited.

Respectfully submitted,

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